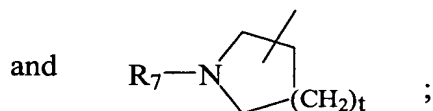
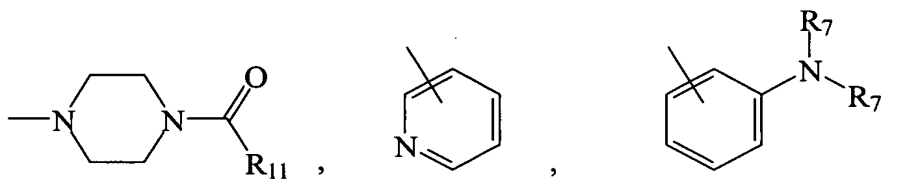
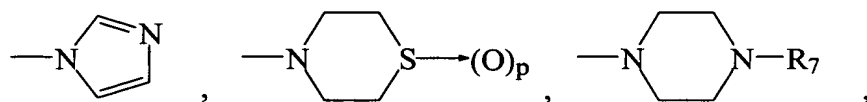
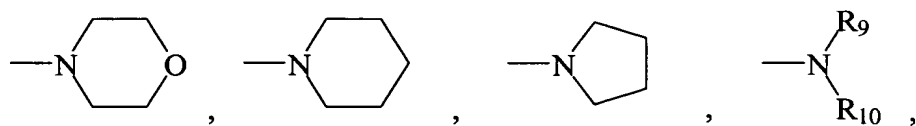
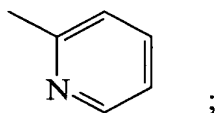
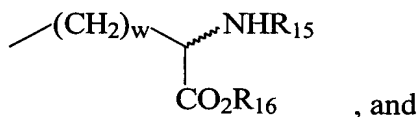
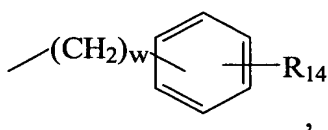
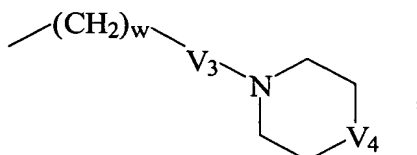
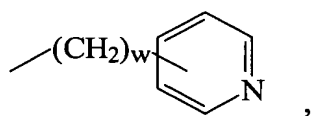
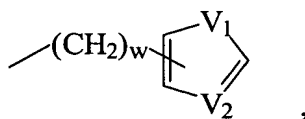
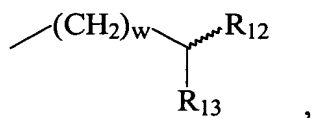


R<sub>7</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or a -(CH<sub>2</sub>)<sub>p</sub>-Ar<sub>2</sub> group wherein Ar<sub>2</sub> is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sub>7</sub>, -N(R<sub>6</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>6</sub>)<sub>2</sub> or -NO<sub>2</sub>;

$R_8$  is hydrogen,  $-C(O)R_7$ , a  $-C(O)-(CH_2)_q-K$  group or a  $-S-G$  group, wherein K is selected from the group consisting of



G is selected from the group consisting of



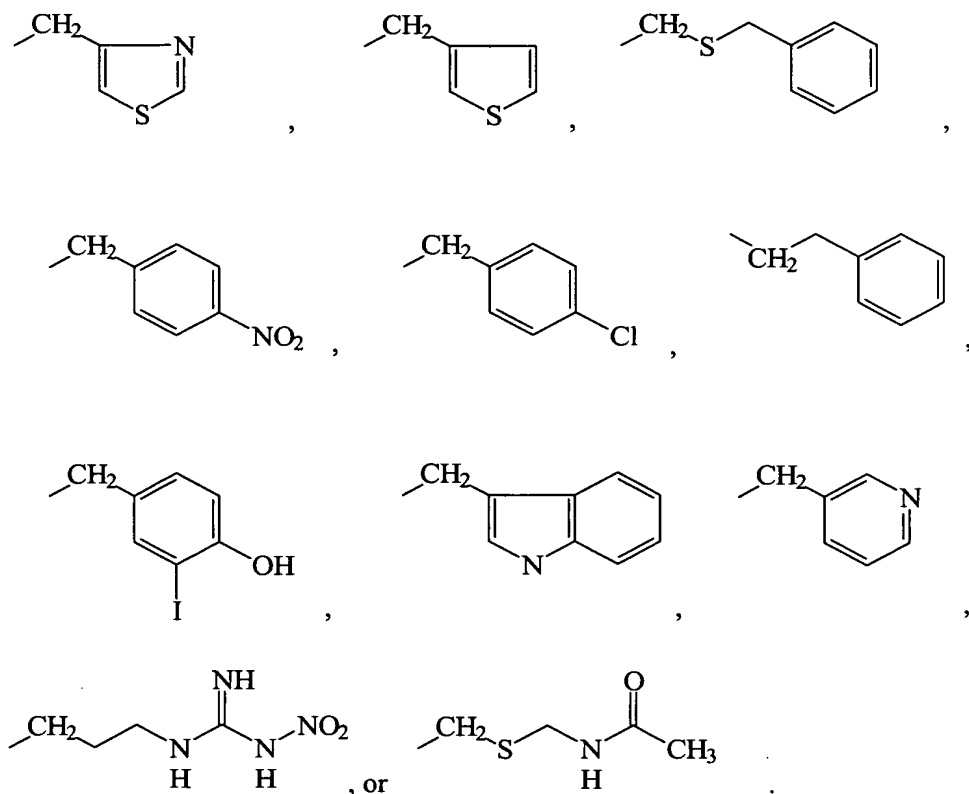
- $\text{R}_9$  and  $\text{R}_{10}$  are each independently  $\text{C}_1\text{-C}_4$  alkyl or a  $\text{---}(\text{CH}_2)_p\text{---Ar}_2$  group;
- $\text{R}_{11}$  is  $\text{---CF}_3$ ,  $\text{C}_1\text{-C}_{10}$  alkyl or a  $\text{---}(\text{CH}_2)_p\text{---Ar}_2$  group;
- $\text{R}_{12}$  is hydrogen,  $\text{C}_1\text{-C}_6$  alkyl,  $\text{---CH}_2\text{CH}_2\text{S(O)}_p\text{CH}_3$ , or arylalkyl;
- $\text{R}_{13}$  is hydrogen, hydroxy, amino,  $\text{C}_1\text{-C}_6$  alkyl, N-methylamino, N,N-dimethylamino,  $\text{---CO}_2\text{R}_{17}$  or  $\text{---OC(O)R}_{18}$  wherein  $\text{R}_{17}$  is hydrogen,  $\text{---CH}_2\text{O---C(O)C(CH}_3)_3$ ,  $\text{C}_1\text{-C}_4$  alkyl, a  $\text{---}(\text{CH}_2)_p\text{---Ar}_2$  group or diphenylmethyl and  $\text{R}_{18}$  is hydrogen,  $\text{C}_1\text{-C}_6$  alkyl or phenyl;
- $\text{R}_{14}$  is 1 or 2 substituents independently chosen from the group consisting of hydrogen,  $\text{C}_1\text{-C}_4$  alkyl,  $\text{C}_1\text{-C}_4$  alkoxy, or halogen;
- $\text{R}_{15}$  is hydrogen,  $\text{C}_1\text{-C}_6$  alkyl or a  $\text{---}(\text{CH}_2)_p\text{---Ar}_2$  group;
- $\text{R}_{16}$  is hydrogen or  $\text{C}_1\text{-C}_4$  alkyl;
- $\text{V}_1$  is O, S, or NH;
- $\text{V}_2$  is N or CH;
- $\text{V}_3$  is a bond or  $\text{---C(O)---}$ ;
- $\text{V}_4$  is  $\text{---}(\text{CH}_2)_w\text{---}$ , O, S,  $\text{NR}_7$ , or  $\text{NC(O)R}_{11}$ ;

X and X' are each independently CH or N;  
m is an integer 2-4;  
n is zero or an integer 1-4;  
p is zero or an integer 1-2;  
q is zero or an integer 1-5;  
t is an integer 1-2;  
w is an integer 1-3; and  
w' is zero or an integer 1; or  
a pharmaceutically acceptable salt, stereoisomer or hydrate thereof.

2. (Original) A compound of claim 1 wherein X is CH.

3. (Original) A compound of claim 2 wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl or a -(CH<sub>2</sub>)<sub>p</sub>-Ar group wherein Ar is phenyl optionally substituted with F, Cl, C<sub>1</sub>-C<sub>4</sub> alkyl, -NO<sub>2</sub>, -NH<sub>2</sub> or -OR<sub>7</sub>; and R<sub>4</sub> is hydrogen.

4. (Currently Amended) A compound of claim 3 wherein R<sub>3</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, [-CH<sub>2</sub>SCH<sub>2</sub>NHCOCH<sub>3</sub>,] or is a compound of the formula



5. (Original) A compound of claim 4 wherein  $\text{R}_5$  is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and  $\text{R}_8$  is hydrogen.

6. (Original) A compound of claim 2 wherein  $\text{R}_1$  is a  $\text{W}-(\text{CH}_2)_m$ - group.

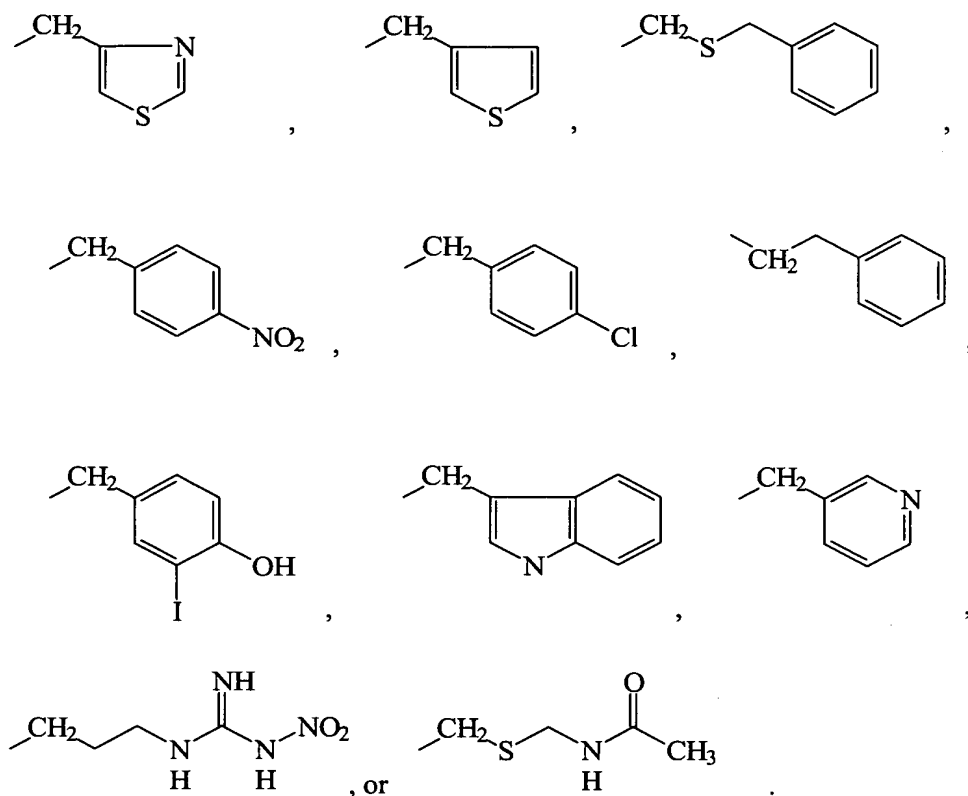
7. (Original) A compound of claim 3 wherein  $\text{R}_1$  is a  $\text{W}-(\text{CH}_2)_m$ - group.

8. (Original) A compound of claim 5 wherein  $\text{R}_1$  is a  $\text{W}-(\text{CH}_2)_m$ - group.

9. (Original) A compound of claim 2 wherein  $\text{R}_1$  is  $\text{C}_1$ - $\text{C}_6$  alkyl.

10. (Original) A compound of claim 3 wherein  $\text{R}_1$  is  $\text{C}_1$ - $\text{C}_6$  alkyl.

11. (Original) A compound of claim 5 wherein  $R_1$  is a  $C_1$ - $C_6$  alkyl.
12. (Original) A compound of claim 2 wherein  $R_1$  is a  $Q-Z-(CH_2)_m$ - group.
13. (Original) A compound of claim 3 wherein  $R_1$  is a  $Q-Z-(CH_2)_m$ - group.
14. (Original) A compound of claim 5 wherein  $R_1$  is a  $Q-Z-(CH_2)_m$ - group.
15. (Original) A compound of claim 1 wherein X is N.
16. (Original) A compound of claim 15 wherein  $R_2$  is  $C_1$ - $C_4$  alkyl or a  $-(CH_2)_p$ -Ar group wherein Ar is phenyl optionally substituted with F, Cl,  $C_1$ - $C_4$  alkyl,  $-NO_2$ ,  $-NH_2$  or  $-OR_8$ ; and  $R_4$  is hydrogen.
17. (Currently Amended) A compound of claim 16 wherein  $R_3$  is hydrogen,  $C_1$ - $C_6$  alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl,  $[-CH_2SCH_2NHCOCH_3]$ , or is a compound of the formula



18. (Original) A compound of claim 17 wherein  $R_5$  is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and  $R_8$  is hydrogen.

19. (Original) A compound of claim 16 wherein  $R_1$  is a  $W-(CH_2)_m$ - group.

20. (Original) A compound of claim 17 wherein  $R_1$  is a  $W-(CH_2)_m$ - group.

21. (Original) A compound of claim 19 wherein  $R_1$  is a  $W-(CH_2)_m$ - group.

22. (Original) A compound of claim 16 wherein  $R_1$  is  $C_1$ - $C_6$  alkyl.

23. (Original) A compound of claim 17 wherein  $R_1$  is  $C_1$ - $C_6$  alkyl.

24. (Original) A compound of claim 19 wherein  $R_1$  is a  $C_1$ - $C_6$  alkyl.

25. (Original) A compound of claim 16 wherein  $R_1$  is a  $Q-Z-(CH_2)_m$ - group.

26. (Original) A compound of claim 17 wherein  $R_1$  is a  $Q-Z-(CH_2)_m$ - group.

27. (Original) A compound of claim 19 wherein  $R_1$  is a  $Q-Z-(CH_2)_m$ - group.

28. (Original) A compound of claim 1 wherein X is CH;  $R_2$  is phenyl, methyl or ethyl;  $R_3$  is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl;  $R_4$  is hydrogen;  $R_5$  is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and  $R_8$  is hydrogen.

29. (Original) A compound of claim 28 wherein  $R_1$  is a  $W-(CH_2)_m$ - group.

30. (Original) A compound of claim 1 wherein X is N;  $R_2$  is phenyl, methyl or ethyl;  $R_3$  is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl;  $R_4$  is hydrogen;  $R_5$  is hydrogen, methyl, ethyl, , propyl, isopropyl, butyl or isobutyl and  $R_8$  is hydrogen.

31. (Original) A compound of claim 30 wherein  $R_1$  is a  $W-(CH_2)_m$ - group.

32. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro- $\alpha$ -mercapto-1,3-dioxo-, [3*S*-[1(*R*\*), 3 $\alpha$ , 5 $\alpha$ ]]-.



33. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro- $\alpha$ -mercapto-1,3-dioxo-, [3*S*-[1(*R*\*), 3 $\alpha$ , 5 $\beta$ ]]-.

34. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-4-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-oxo-1-(phenylmethyl)-1*H*-1,4-diazepin-6-yl]-1,3-dihydro- $\alpha$ -mercapto-1,3-dioxo-, [6*S*-[4(*R*\*), 6*R*\*(*R*\*)]]-.

35. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

36. (Original) A method of inhibiting matrix metalloproteinase in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

37. (Original) A method of inhibiting MMP-induced tissue disruption and/or MMP-induced tissue degradation in a patient in need thereof which comprises administering to the patient and effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

38. (Original) A method of treating rheumatoid arthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

39. (Original) A method of treating osteoarthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

40. (Original) A method of treating a chronic inflammatory disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

41. (Original) A method of treating a neoplastic disease state in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

42. (Original) A method of treating a cardiovascular disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

43. (Original) A method of claim 42 wherein said cardiovascular disorder is atherosclerosis.

44. (Original) A method of treating corneal ulceration in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

45. (Original) A method of treating gingivitis or periodontal disease in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

46. (Original) A method of treating multiple sclerosis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

47. (Original) A method of treating chronic obstructive pulmonary disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.